



ORIGINAL ARTICLE

Endoscopic tightening of the cardia mucosa in gastroesophageal reflux disease: A case series of 120 patients up to 1-year follow-up

Zhenhua Li[†], Yongliang Li[†], Yue Wu^{2†}, Mingyan Li¹, Zhaobin Yan¹, Shanwen Nie¹, Zhitao Liang¹, Bo Li¹, Peiwen Zhu¹, Peilin Cui², Qinsheng Zhang^{1*}

¹Department of Hepatobiliary and Spleen and Gastroenterology, Henan Provincial Hospital of Traditional Chinese Medicine, Zhengzhou, China,

²International Medical Services, Beijing Tiantan Hospital of Capital Medical University, Beijing, China

[†]These authors contributed equally to this work.

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**Corresponding author:*

Qinsheng Zhang

Department of Hepatobiliary and Spleen and Gastroenterology, Henan Provincial Hospital of Traditional Chinese Medicine, Jinshui District, Zhengzhou, Henan Province, China.

E-mail: 80792825@qq.com

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ABSTRACT

Background and Aim: A technique of endoscopic tightening of the cardia mucosa for the treatment of gastroesophageal reflux disease (GERD) was developed and its clinical efficacy was observed.

Methods: 120 patients with GERD who underwent endoscopic tightening surgery from December 2017 to December 2019 were included in this study. GERD-Q score and constitution type of patients were evaluated preoperatively and at 1 month, 3 months, 6 months, and 1 year after surgery. In addition, effectiveness and side effects of the procedure were graded based on gastroesophageal flap valve (GEFV) function.

Results: GERD-Q score of 1 month, 3 months, 6 months, and 1 year after surgery were significantly decreased ($P < 0.01$) compared with preoperative score. There were no significant differences between GERD-Q score of 1 month, 3 months, 6 months, and 1 year after surgery. The surgery proves to be effective in all GEFV grades, especially in Hill-III.

Conclusion: Endoscopic tightening is an effective method for the treatment of patients with GERD, especially of Hill-III patients. Attention should be paid to cardia width, ligation ring depth, and ring number during operation.

Relevance for Patients: ETCM is a safe endoscopic procedure with minimal trauma, which has been proved effective for patients who are diagnosed with GERD.

1. Introduction

Gastroesophageal reflux disease (GERD) is a common disorder, with symptoms and/or complications caused by reflux of gastric contents into the esophagus [1-3]. Acid reflux and heartburn are the most common symptoms [4] and are often accompanied by chest pain, upper abdominal pain or burning, and belching; cough, throat discomfort, asthma, and dental erosion may be present in some patients. Three clinical types of GERD have been delineated: erosive esophagitis, non-erosive reflux disease, and Barrett's esophagus. The current consensus on the pathogenesis of this disease is that there is digestive dyskinesia caused by a variety of factors [5-7], with weakening of the anti-reflux defense mechanism and attack of the refluxate on the esophageal mucosa. The refluxate may contain variable amounts of gastric acid, bile salts, and pancreatic enzymes.

The long-term medical treatment of GERD often is unsatisfactory. Therefore, surgical treatments, such as total fundoplication, partial fundoplication, and cardia fixation, are often used [8]. In recent years, endoscopic methods for the surgical treatment of GERD

have received increasing attention, but these methods have not yet been widely used clinically [9-12]. Our team has been focused on the treatment of GERD, and we have got satisfying results from combination of Chinese and Western medicine in treating this disease. Herein, we report our experience with endoscopic tightening of the cardia mucosa (ETCM) in the treatment of GERD in a consecutive series of patients and analyze indication and clinical effectiveness of this procedure, which provide insightful ideas for further study on effective treatment of GERD by combined therapy of Chinese and Western medicine.

2. Materials and Methods

2.1. Subjects

120 patients (73 males and 47 females) with GERD were hospitalized from December 2017 to December 2019 in the Department of Gastroenterology and Hepatology at Henan Traditional Chinese Medicine (TCM) Hospital. Patients are aged between 22 and 84-year-old. The experimental protocol was approved by the Medical Ethics Office of Henan Provincial Hospital of TCM, and all patients gave informed consent. As far as GEFV grades, 31 patients of II grade, 53 patients of III grade, and 36 patients of IV grade.

2.2. Disease diagnosis criteria

The diagnostic criteria for GERD were based on the 2014 Chinese expert consensus on GERD [13] and a study by Li et al. [14] The criteria were as follows: symptoms of reflux and/or heartburn; endoscopic evidence of erosive esophagitis, Barrett's esophagus, or normal mucosa; esophageal 24-h pH <4.0 for greater than 1 h; and resting pressure in the lower esophagus <6 mm Hg.

2.3. Inclusion and exclusion criteria

Inclusion criteria were as follows: 1) patients who met the diagnostic criteria for GERD; 2) patients with poor response to proton pump inhibitors for 8 weeks or unwilling to take them for a long time; and 3) patients who agreed and signed the informed consent of both the operation and follow-up from 1 month, 3 months, 6 months, and 12 months after operation.

Exclusion criteria were: 1) patients who were diagnosed with early cancer; 2) patients who have undergone stomach surgeries before, such as fundoplication; 3) patients with severe cardiovascular, cerebrovascular, lung, or kidney diseases; and 4) patients with poor compliance who are unable to cooperate with follow-up.

2.4. Scoring criteria and response evaluation criteria

GEFV grading is according to the Hill's classification [15]: Grade I: fold of tissue tightly surrounds the endoscope; Grade II: fold is prominent but there is intermittently opening and closing around the scope; Grade III: fold is not obvious and the diaphragmatic hiatus is freely open, with no or minimal sliding hiatal hernia visible; Grade IV: fold disappeared, and the diaphragmatic hiatus increased significantly, showing a well-defined sliding hiatal hernia.

Based on GERD-Q scoring standard and patients' satisfaction, efficacy evaluation was graded as markedly effective (remission rate \geq ef), effective (remission rate 51-90%), moderate (remission rate 11-50%), or ineffective (remission rate \leq or).

Other indicators such as ligation ring number, times of operation, and the classification of constitution in TCM are also used to evaluate the effectiveness of the operation.

2.5. Treatment

Patients who met the selection criteria were treated with ETCM. For the procedure, the patient was placed in the left lateral decubitus position. Under general anesthesia, routine esophagogastroduodenoscopy was performed with a gastroscope (CV-260, Olympus, Japan). Images were taken, and the endoscope was retracted. A Cook six-shooter ligator (MBL-6-F, Cook Medical, US) was installed on the front end of the gastroscope, which was advanced to the fundus through the mouth. The gastroscope was retroflexed, and the mucous membrane around the cardia opening of the gastric fundus was suck tightly onto the scope. One to four ligatures were applied, based on the degree of tightening needed. The gastroscope was retroflexed in the cardia, and the cardia mucosa was ligated again along the squamocolumnar junction (SCJ). Similarly, one to four ligations were done, based on the degree of tightening needed. The patients fasted for 24 h after surgery, and then started semi-liquid food on day 3 after surgery. During hospitalization, the patients routinely received intravenous pantoprazole 40 mg twice daily (Yangtze River Pharmaceutical Group, Taizhou, Jiangsu Province, China), agents to protect the gastric mucosa and gastric motility medications taken orally, and sucralfate oral solution 10 mL 3 times daily for 14 days. Follow-up was performed at 1 month, 3 months, 6 months, and 1 year after surgery.

2.6. Statistical methods

The IBM SPSS Modeler V23.0 statistical software was applied. Analysis of variance (ANOVA) was used for statistical analysis of GERD-Q score. Measurement data are displayed as the mean \pm SD. $P < 0.05$ was considered statistically significant.

3. Results

3.1. GERD-Q scores of patients before and after surgery

One-way repeated measures ANOVA is used to compare preoperative and post-operative GERD-Q score. GERD-Q score of 1 month, 3 months, 6 months, and 1 year after surgery was significantly decreased ($P < 0.01$) compared with preoperative score. There were no significant differences between GERD-Q of 1 month, 3 months, 6 months, and 1 year after surgery ($P > 0.05$) (Figure 1).

3.2. Endoscopic evaluation of endoscopic tightening before, during, and after endoscopic treatment

Photographs illustrating the endoscopic appearance of the gastroesophageal junction in a patient are presented in Figures 2-4.

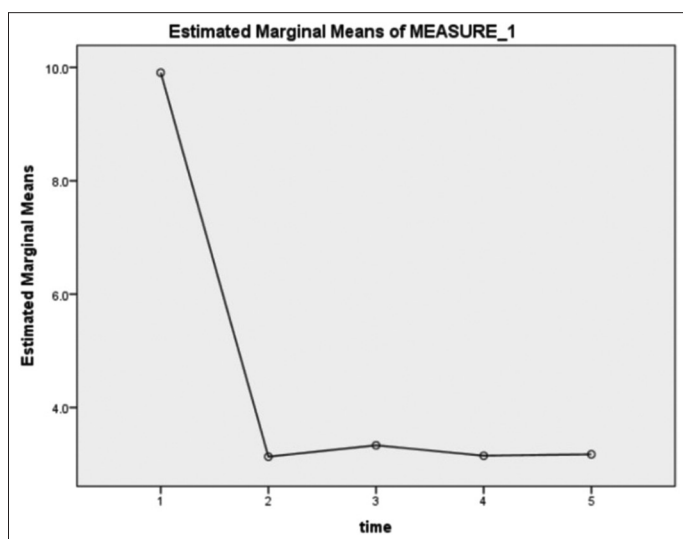


Figure 1. Statistical results before and after ETCM (1-before operation; 2-1 month after operation; 3-3 months after operation; 4-6 months after operation; and 5-12 months after operation).

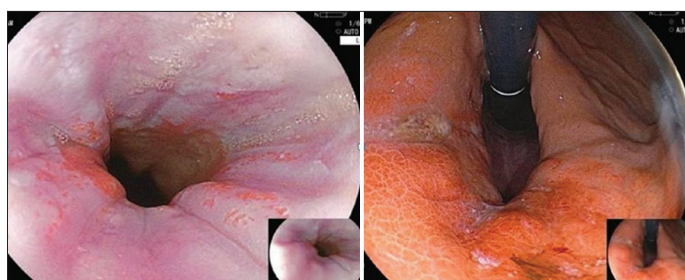


Figure 2. Endoscopic images before the endoscopic tightening procedure, revealing a patulous gastroesophageal junction and esophagitis. Left, straight-on view; right, retroflexed view.

Before the procedure, there is evidence of esophagitis, and the gastroesophageal junction is patulous. One month after the procedure there is no evident esophagitis, and the gastroesophageal junction is closed. The ligation bands have fallen off, and scar has formed; the mucosa at the gastroesophageal junction is drawn together, tightening the opening.

3.3. Efficacy assessment before and after ETCM

After ETCM, the patient's reflux, heartburn, and retrosternal burning sensation, as well as cough and asthma symptoms in some patients, were significantly improved. Based on the standard talked above, the operation is markedly effective in 52 patients, effective in 24 patients and moderate in 24 patients. Overall effective rate is about 83.33%, effective rate of II grade is 80.65%, III grade is 90.57%, and IV grade is 75% (Table 1).

3.4. Analyze of side effects and ineffective patients

Two out of 120 patients (1.67%) showed complications after operation, they complained of dysphagia and hoarseness, and endoscope showed slightly narrowing of the cardia. These

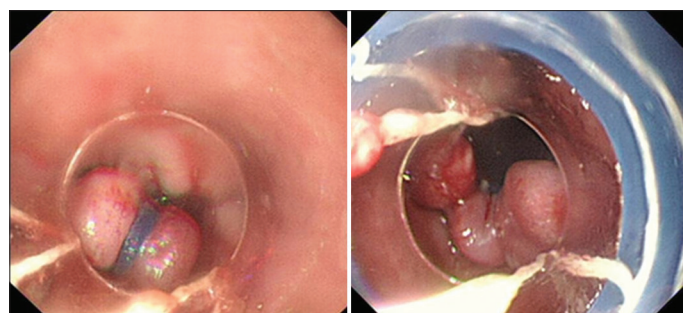


Figure 3. Endoscopic images during the endoscopic tightening procedure.

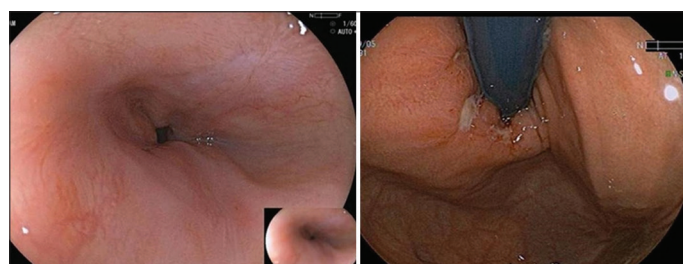


Figure 4. Endoscopic images after the endoscopic tightening procedure, revealing a tightened gastroesophageal junction and no esophagitis. Left, straight-on view; right, retroflexed view.

Table 1. Evaluation before and after ETCM.

Hill grade	Markedly effective	Effective	Moderate	Ineffective
II	15	2	8	6
III	31	9	8	5
IV	36	19	5	9

Table 2. Ligation ring number and times of operation.

Hill grade	Ligation ring number	Times of operation
II	4.26±0.84	1.03±0.18
III	4.36±0.87	1.17±0.42
IV	5.08±1.75	1.11±0.31

two patients are all of Hill II grade with ligation ring number of 4 and 5 (Table 2).

Results also showed that the operation was ineffective in 20 patients. Based on the classification of constitution in TCM, the top three constitutions of these patients are Qi stagnation type, Damp-heat type, and Yang deficient type. In addition, Qi stagnation type accounts for 50% of these patients.

4. Discussion

4.1. ETCM is developed based on the cause of GERD, which proves to be markedly effective

GERD is a digestive motility disorder. The main mechanism of this disease is relaxation of the lower esophageal sphincter (LES) or damage of anti-reflux barrier, which are closely related with hiatal hernia, lower pressure of LES, weakened esophageal

clearance, and delayed gastric emptying. The anatomical integrity of esophageal-gastric junction (EGJ) may be the main reason how abnormal esophageal acid clearance progress into esophagitis [16]. Some research showed that long-segment ligation of the mucosa and part of the muscle layer above and below EGJ can further increase the pressure of LES and cardia.

ETCM is by ligation along the SCJ through endoscope, loss of cardia mucosa forms scar, which increases the pressure of LES and prevents gastroesophageal reflux. In this experience with ETCM in the treatment of GERD in a consecutive series of patients, post-operative GERD-Q score had significantly decreased compared with pre-operative values ($P < 0.01$), which proves that ETCM is an effective method for treating GERD; there were no significant differences between GERD-Q score of 1 month, 3 months, 6 months, and 1 year after surgery, which indicates that the therapeutic effect of ETCM is stable. The operation is simple and safe, with minimal trauma. The procedure has been video demonstrated at national digestive and digestive endoscopy conferences, has been widely recognized by national endoscopy experts, and has been patented in China.

4.2. ETCM is found effective in different grade of GEFV, but further studies are needed to elucidate the mechanism

GEFV is considered a barrier to esophageal reflux at EGJ, different grading can accurately reflect the function of the anti-reflux barrier at the gastroesophageal junction. As the GEFV grade increases, the pressure of LES and anti-reflux function decreases, and the incidence of reflux esophagitis and Barrett's esophagus both increases, which requires more surgical intervention. Based on our results of different GEFV grade, ETCM is effective for Hill-II/III/IV patients, especially for Hill-III patients; in addition, the operation is not only effective for patients with abnormal cardia relaxation (Hill-III/IV), but also for patients with cardia that is not loose (Hill-II), which indicates that ETCM increases the pressure of LES, but whether it also initiates other mechanisms remains to be confirmed by further studies. By analyzing side effects, times of operation and operation style in ineffective patients, it is suggested that the width of the cardia, the depth of ligation and ligation ring number affect the therapeutic effect of operation. For Hill-II patients, attention should be paid to the depth and loop of ligation to avoid side effects.

4.3. Different constitution types affect the prognosis of GERD, so it is imperative to strengthen the health management before and after surgery

Changes of lifestyle and health education are the basis for GERD treatment and prevention, and they should run through the entire process of disease treatment and management. Therefore, providing scientific health education and strengthening symptom management are the keys to control reflux symptom, reduce the incidence of complications, and improve patient's life qualities. Based on the follow-up of our study, different constitution type affects the prognosis of the disease, namely, Qi stagnation type, Damp-heat type, and Yang deficient type.

We recognize that our study has limitations. It is a short-term, single-center study of a relatively small population. Longer term studies in multiple centers with larger populations are needed to accurately assess the efficacy and safety of ETCM in the treatment of GERD. Moreover, the assessment of subjective and objective responses to ETCM was not done in a blinded manner; thus, we cannot be certain that there was no inadvertent bias in interpretation of results.

5. Conclusion

ETCM in the treatment of GERD appears to be an effective and safe procedure, especially for Hill-III patients. During operation, it is important to concentrate on cardia width, ligation ring depth, and ring number. In addition, strengthen the health management of patients before and after operation is crucial for the treatment of GERD.

Conflict of Interest

The authors declare that there is no conflict of interest.

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Research Ethics and Patient Consent

The experimental protocol was approved by the Medical Ethics Office of Henan Provincial Hospital of Traditional Chinese Medicine, and all subjects gave informed consent.

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